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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

IMMUNOMEDICS, INC., Plaintiff, V. ROGER WILLIAMS MEDICAL CENTER, RICHARD P. JUNGHANS, M.D., Ph.D., STEVEN C. KATZ, M.D., ABC ENTITIES 1-10 Defendants.	C.A. No. 2:15-cv-04526-JLL-JAD

DEFENDANTS' OPENING CLAIM CONSTRUCTION BRIEF

Pursuant to the scheduling order entered by the Court, Defendants Roger Williams Medical Center, Richard P. Junghans, M.D., Ph.D, and Steven C. Katz, M.D. (collectively "Defendants") hereby submit this opening claim construction brief in support of their position that the single claim term to be construed – "effective amount" or "effective immunostimulatory amount" – is indefinite and not subject to a reasonable construction. Because the disputed claim term fails to inform those skilled in the art about the scope of the invention with reasonable certainty, the term should be deemed indefinite and not subject to

a reasonable construction.

THE PATENTS-IN-SUIT

The Plaintiff has asserted three patents in this lawsuit; however, the disputed claim term appears in only two of the patents-in-suit – United States Patent Nos. 6,676,924 (the "'924 Patent") and 6,926,893 (the "'893 Patent"). Copies of those patents are attached hereto as Exhibits A and B.

The '924 Patent, entitled "CDR-Grafted Type III Anti-Cea Humanized Mouse Monoclonal Antibodies," contains 27 claims, four of which plaintiff claims that Defendants have infringed. The disputed claim term appears in claims 1, 14 and 23 of the '924 Patent as follows:

What is claimed is:

1. A method for treating a patient comprising administering a conjugate to said patient in an ***effective amount*** for treatment, wherein said conjugate comprises:

a therapeutic agent bound to a humanized Class III, anti-CEA, monoclonal antibody (mAb) or a fragment thereof…[1].

14. A method for diagnosing a patient comprising administering a conjugate to said patient in an ***effective amount*** for diagnosis, wherein said conjugate comprises:

a diagnostic agent bound to a humanized Class III, anti-CEA, monoclonal antibody (mAb) or a fragment thereof….

23. A method for treating a patient comprising administering a humanized Class III, anti-CEA, monoclonal antibody (mAb) to said patient in an ***effective amount*** for treatment, wherein said m/Ab comprises:

a humanized Class III, anti-CEA, monoclonal antibody (mAb)….

The '893 Patent, entitled "Multi-Stage Cascade Boosting Vaccine," contains six (6)

[1] The remainder of the claim identifies the specific amino acid sequence of the monoclonal antibody portion of the conjugate. Defendants provide the truncated claims above because that sequence does not affect the construction of "effective amount."

claims and the disputed claim term appears in claims 1 and 4 as follows:

What is claimed is:

1. A method for inducing a cellular immune response in a patient against a tumor that expresses carcinoembryonic antigen (CEA), said method comprising:

administering an ***effective immunostimulatory amount*** of transfected T cells to a patient; and subsequently administering at least one cytokine to said patient; wherein said transfected T cells are produced by obtaining T cells from the patient and transfecting said T cells with an expression vector to obtain said transfected T cells; wherein said expression vector comprises a DNA molecule encoding either a chimeric immunoglobulin/T cell receptor or a chimeric immunoglobulin/CD3 protein, and wherein said immunoglobulin-encoding portion of said DNA molecule encodes the variable regions of a Class III anti-CEA antibody, wherein the Class III anti-CEA antibody is MN-14 or humanized MN-14, and further wherein the variable regions of the O. and flpolypeptide chains of said T cell receptor are replaced by said variable regions of the antibody.

4. A method for inducing a cellular immune response in a patient against a tumor that expresses carcinoembryonic antigen (CEA), said method comprising:

administering an effective immunostimulatory amount of transfected T cells to a patient; and subsequently administering at least one cytokine to said patient; wherein said T cells are produced by obtaining T cells from the patient and transfecting said T cells with an expression vector to obtain said transfected T cells; wherein said expression vector comprises a DNA molecule encoding either a chimeric immunoglobulin/Tcell receptor or a chimeric immunoglobulin/CD3 protein, and wherein said immunoglobulin-encoding portion of said DNA molecule encodes the variable regions of an anti-idiotypic antibody that recognizes a Class III anti-CEA antibody, wherein the anti-idiotype antibody is WI2, and further wherein the variable regions of the C. and f polypeptide chains of said T cell receptor are replaced by said variable regions of the antibody.

ARGUMENT

A. The Law of Claim Construction

Claim construction is a question of law for the Court, not a jury, to decide. *Markman v. Westview Instruments, Inc.*, 517 U.S. 370, 372 (1996). "It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc) (citations and quotations omitted). In view of patents' public notice function, defining the metes and bounds of the monopoly granted, courts should rely only on intrinsic evidence — the claims, specification, and prosecution history — to construe the claims. *See Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 987 (Fed. Cir. 1995) (en banc), *aff'd*, 517 U.S. 370 (1996) ("[I]t is from the public record that a court should seek in a patent infringement case to find the meaning of claim language.").

Similarly, the words of a claim "are generally given their ordinary and customary meaning," *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582 (Fed. Cir. 1996), which "is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention." *Phillips*, 415 F.3d at 1313 (citations omitted). The claims are not read in a vacuum, however. The specification "is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term." *Vitronics*, 90 F.3d at 1582; *accord Phillips*, 415 F.3d at 1313 ("Importantly, the person of ordinary skill in the art is deemed to read the claim term not only in the context of the particular claim in which the disputed term appears, but in the context of the entire patent, including the specification."). "Ultimately the interpretation to be given a term can only be determined and confirmed with a full understanding of what the inventors actually invented and intended to envelop with the claim." *Phillips*, 415 F.3d at 1316 (citations omitted).

Here, the sole issue for the Court to decide is whether the disputed claim term is

indefinite and not subject to a reasonable construction, or is definite and should be given its plain and ordinary meaning. In *Nautilus, Inc. v. Biosig Instruments, Inc.*, 134 S.Ct. 2120, 2129 (2014), the United States Supreme Court lessened the standard for finding claim terms indefinite. Specifically, the Supreme Court held that the definiteness requirement of 35 U.S.C. § 112, ¶ 2 requires that "a patent's claims, viewed in light of the specification and prosecution history, inform those skilled in the art about the scope of the invention with reasonable certainty." *Id.* An indefiniteness inquiry requires a delicate balance between precision and uncertainty:

> [A] patent must be precise enough to afford clear notice of what is claimed, thereby 'appris[ing] the public of what is still open to them.' Otherwise there would be '[a] zone of uncertainty which enterprise and experimentation may enter only at the risk of infringement claims.' And absent a meaningful definiteness check, we are told, patent applicants face powerful incentives to inject ambiguity into their claims. . . . Eliminating that temptation is in order, and 'the patent drafter is in the best position to resolve the ambiguity in . . . patent claims.'
>
> *Id.* at 2128-29 (internal citations omitted).

The Federal Circuit has ruled that terms of degree, such as the disputed claim term, "are problematic if their baseline is unclear to those of ordinary skill in the art." *Liberty Ammunition, Inc. v. United States*, 2016 U.S. App. LEXIS 15762, *13 (Fed. Cir. 2016) ("We especially take caution when presented with terms of degree following the Supreme Court's decision in *Nautilus*…). Although terms of degree are not "inherently indefinite," the Federal Circuit has "recognized that claims having terms of degree will fail for indefiniteness unless they 'provide objective boundaries for those skilled in the art' when read in light of the specification and the prosecution history." *Id., citing Interval Licensing LLC v. AOL, Inc.*, 766 F.3d 1364, 1370-71 (Fed. Cir. 2014), *cert. denied*, 136 S. Ct. 59 (2015). There is "an indefiniteness problem if the claim language 'might mean several different things and 'no informed and confident choice is available among the contending definitions.'" *Interval Licensing* at 1371 (citations omitted). Claims must provide "objective boundaries" rather than depending "on the unpredictable

vagaries of any one person's opinion." *Id*. Patent claims have been found to be indefinite where the specification discloses multiple methods for evaluating a claim limitation without guidance to a person of ordinary skill in the art about which method to use. *Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 789 F.3d 1335, 1344-45 (Fed. Cir. 2015).

B. The Disputed Claim Terms Are Indefinite

Nothing in the specifications or any of the other evidence relied upon by plaintiff provides objective boundaries for those skilled in the art as to the term "effective amount" or "effective immunostimulatory amount." In support for its position that the disputed term should be given its plain and ordinary meaning, plaintiff cites to a single portion of the specification (beyond the claim language itself) for each patent. For the '924 Patent, the single citation reads as follows:

> As noted above, for purposes of therapy, a humanized antibody conjugate and a pharmaceutically acceptable carrier are administered to a patient in a therapeutically effective amount. A combination of a conjugate and a pharmaceutically acceptable carrier is said to be administered in a "therapeutically effective amount" if the amount administered is physiologically significant. An agent is "physiologically significant" if its presence results in a Detectable change in the physiology of a recipient patient. A targeted therapeutic agent is "therapeutically effective" if it delivers a higher proportion of the administered dose to the intended target than accretes at the target upon systemic administration of the equivalent untargeted agent. ('924 Patent, Col. 10, lines 53-65).

Plaintiff relies on a similar provision in the '893 Patent, which reads as follows:

> For purposes of therapy, antibodies or fragments are administered to a mammal in a therapeutically effective amount. An antibody preparation is said to be administered in a "therapeutically effective amount" if the amount administered is physiologically significant. An agent is physiologically significant if its presence results in a detectable change in the physiology of a recipient mammal. In particular, an antibody preparation of the present invention is physiologically significant if its presence invokes a

humoral and/or cellular immune response in the recipient mammal. ('893 Patent, Col. 13, lines 43-52).

These terms define "effective amount" in a circular fashion that does not clarify the scope of "effective amount" and "effective immunostimulatory amount." For instance, in the '924 Patent specification a "therapeutically effective amount" is said to be an amount that is "physiologically significant." '924 Patent, Col. 10, lines 56-59. An agent is said to be "physiologically significant" if its presence results in "a detectable change in the physiology of a recipient patient." '924 Patent, Col. 10, lines 59-61. However, nothing in the specification teaches one skilled in the art as to what constitutes a "detectable change" in the physiology of a recipient patient or how to measure for any potential "detectable change," or when to look for such a change. The specification for the '893 Patent contains similar language that provides a similarly circular definition of "effective amount." '893 Patent, Col. 13, lines 45-52.[2] The cited specification language introduces more ambiguity as to the meaning of the disputed claim term, and leaves one skilled in the art to his/her own devices to determine what constitutes a "detectable change" and what measurement to utilize in making that determination.

There are many potential physiological effects that might be caused by administration of an antibody conjugate, including therapeutic effects, beneficial side effects, and deleterious side effects. *See, e.g.,* '924 patent , Col. 11, lines 23-24, 34-36 (referring to "dose-limiting side effects," "beneficial side effects," "therapeutic effect" and "deleterious side effects"); Col. 9, lines 63-Col. 10, line 5 (referring to "negative immune reactions"); Col. 12, lines 14-20 (referring to "adverse side effects"). Even if a person of ordinary skill in the art chose to focus on a therapeutic effect, the claims fail to specify what disease is being treated, making it

[2] Significantly, although claims 1 and 4 of the '893 Patent use the term "effective immunostimulatory amount," that term does not appear in the patent outside of the claim language.

impossible to classify a particular physiological effect as therapeutic or irrelevant. The specification acknowledges that the therapeutic dose "depend[s] on the status of the patient and the mode of administration." '924 patent, Col. 10, lines 26-31.

Compounding the confusion, the specification provides no guidance on *when* to look for physiological effects. Any given antibody conjugate could have no physiological effect minutes after administration of a single dose, but an effect might be detected after an hour, a day or a week. Alternatively, multiple doses of the same antibody conjugate might cumulatively produce a detectable effect whereas a single dose was ineffective. Is the claimed "effective amount" the amount of each dose, or the cumulative amount of conjugate administered? Could a doctor or scientist infringe after administering a single, ineffective dose, or could infringement only occur after multiple doses were administered?

The specification of the '924 patent offers conflicting definitions of what may be considered "therapeutically effective." According to the patent, any amount of a therapeutic agent is considered "therapeutically effective" as long as a higher proportion of the dose is delivered to the target compared to systemic administration of the untargeted agent. '924 patent, Col. 10, lines 66 – Col. 11, line 1. Under this definition, *no* therapeutic or physiological effect is required. The specification even acknowledges that the antibody conjugate may not be therapeutically effective by itself, but may be if "administered in combination with other therapeutic agents or as part of a broader treatment regimen." '924 patent, Col. 10, line 66- Col. 11, line 1. According to this part of the specification, a "therapeutically effective amount" may be any amount of the conjugate, even one without a detectable physiological effect.

Thus, what constitutes an "effective amount" is a non-existent, or at best, a moving target – dependent on what one skilled in the art deems a "detectable change" based on the

measurement adopted by that person. The Federal Circuit has held that terms of degree that are moving targets are indefinite. *See, e.g. Icon Health & Fitness, Inc. v. Polar Electro Oy*, 2016 U.S. App. LEXIS 14482, *16 (Fed. Cir. 2016) ("In-band" cannot provide a basis, therefore, to determine which communications are "out-of-band" if the terms are a moving target); *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1341 (Fed. Cir. 2003) ("one must know what the glycosylation of uEPO is with certainty before one can determine whether the claimed glycoprotein has a glycosylation different from that of uEPO."). Here, there are multiple possible meanings of "detectable change" and multiple possible methods for measuring whether there has been a "detectable change." The patents provide no guidance to a person of ordinary skill in the art about the meaning of the term or which method to employ to measure it. *See Teva Pharms. USA, Inc. v. Sandoz, Inc.*, 789 F.3d at 1344-45 (Fed. Cir. 2015).

In short, in order to overcome an indefiniteness challenge, "the patent and prosecution history must disclose a single known approach or establish that, when multiple known approaches exist, a person having ordinary skill in the art would know which approach to select." *Dow Chemical v. Nova Chemical Corp. (Canada)*, 803 F.3d 620, 630 (Fed. Cir. 2015). The '924 and '893 Patents fail to do so with respect to the claim term "effective amount" or "effective immunostimulatory amount." Thus, that term is indefinite.

CONCLUSION

For all of these reasons, Defendants respectfully request that this Court find that the disputed claim term is indefinite and not subject to a reasonable construction.

Respectfully submitted,
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CERTIFICATE OF SERVICE

This is to certify that a true and correct copy of the foregoing

DEFENDANTS' OPENING CLAIM CONSTRUCTION BRIEF

is to be electronically filed. Notice of this filing will be sent to all parties by operation of the Court's electronic filing system. Parties may access this filing through the Court's system.

September 27, 2016
Date

/s/Christina Saveriano
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